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Brief Clinical Report

Diffuse Polymicrogyria Associated With an Unusual Pattern of Multiple Congenital Anomalies Including Turribrachycephaly and Hypogenitalism

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A newborn male infant born to consanguineous parents was found to have diffuse polymicrogyria associated with an unusual pattern of congenital anomalies including microbrachycephaly, turricephaly, blepharophimosis, microstomia with maxillary retrusion and mandibular prognathism, micropenis with cryptorchidism, camptodactyly and adducted thumbs, and a progeroid appearance.

The combination of manifestations in our patient represents a unique form of polymicrogyria with congenital anomalies, probably representing a new syndrome.

KEY WORDS: polymicrogyria, lissencephaly, brachymicrocephaly, progeria, micropenis, adducted thumb, early death

INTRODUCTION

We report on a child with diffuse polymicrogyria, prominent sylvian fissure, and diffuse abnormal signal in the white matter with multiple congenital anomalies such as short stature, brachymicrocephaly with turricephalic head configuration, low posterior hair line, blepharophimosis, microstomia, maxillary retrusion and mandibular prognathism, a progeroid appearance, diminution of subcutaneous fat tissue, microgenitalia, camptodactyly, and adducted thumbs.

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Dedicated to Jürgen W. Spranger on the occasion of his 65th birthday with admiration and best wishes.

Although several syndromes with polymicrogyria or lissencephaly associated with multiple congenital anomalies have been reported [for review, see Dobyns and Truwit, 1995], none of these reports describe this unique pattern of multiple congenital anomalies associated with diffuse polymicrogyria, present in our patient.

CLINICAL REPORT

D.B. was the first child of healthy German, consanguineous parents (1st cousins). The sister of the father had a unilateral cleft of lip and palate. The mother had a healthy child from a previous marriage.

Intrauterine growth retardation was noted by ultrasonography. Delivery was at 37 weeks by cesarean section because of a pathologic cardiotocography.

Birthweight was 1.640 g (<3rd centile), length was 41 cm (<3rd centile) and OFC was 28 cm (<3rd centile). Apgar scores were 7 and 8 at 5 and 10 minutes, respectively. Immediately after birth the child needed artificial ventilation due to respiratory insufficiency. Routine chromosome analysis (G-banded) showed a 46, XY karyotype. Serology revealed no evidence of intrauterine infection.

The boy was found to have microbrachycephaly with turricephalic head configuration, a receding forehead, low posterior hair line, and a large anterior fontanelle (Fig. 1a,b). He had blepharophimosis, sparse eyelashes, and slight upslant of palpebral fissures. His midface was hypoplastic including a low nasal bridge, microstomia with narrow lips, a normal tongue, and a median soft palate. There was also mandibular prognathism and maxillary retrusion. The ears were somewhat large and the superior half of the helix was incompletely folded. The boy had a progeroid appearance. Subcutaneous fat of the skull, and trunk was diminished. The internipple distance was 8 cm (0.5 cm above the mean).

He had a micropenis, hypoplastic scrotum, and cryptorchidism (Fig. 2), adducted thumbs (Fig. 3), transverse palmar creases, ulnar deviation of the fingers, and camptodactyly and hypoplastic nails of the feet.

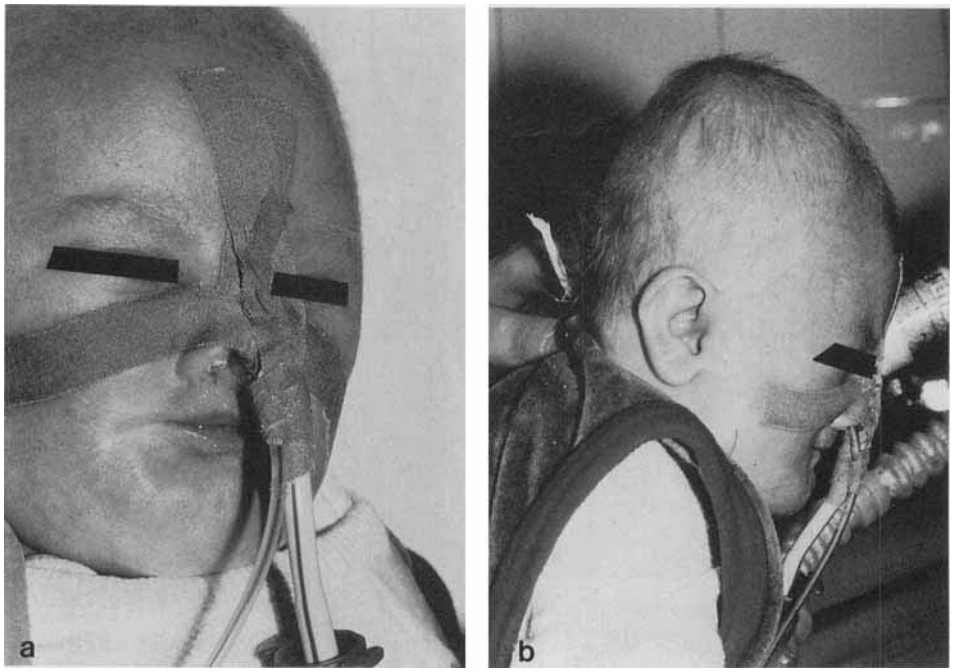

Fig. 1. **a,b:** Pat D.P. at 2 months, frontal and lateral aspect. Note microbrachycephaly with turricephalic head configuration, low posterior hair line, large ears, mandibular prognathism, and maxillary retrusion.

The infant had muscular hypertonia of the limbs bilaterally and hypotonia of the trunk.

An abdominal ultrasound investigation showed an atypical localization of the abdominal aorta to the right; both kidneys, liver, spleen, and pancreas were normal.

Echocardiography was normal. Examination of the eye showed no pathologic changes of the retina, lens and iris. The EEG displayed a nonspecific disturbance of background rhythm. A MRI scan, performed at age 3 months, showed diffuse polymicrogyria, an abnormal extension of the sylvian fissure into the convexity (Fig. 4) and diffuse abnormal signal in the white matter (Fig. 5). The cerebellum was of relatively normal size given the size of the brain.

D.P. died at 4 months never having been able to breathe without mechanical support.

DISCUSSION

Thus our patient had diffuse polymicrogyria with diffuse abnormal signal of the white matter, microbrachycephaly with turricephalic head configuration, facial abnormalities, adducted thumbs, and microgenitalia. An extended search by using the London Dysmorphology Database [Winter and Baraitser, 1995] and the POSSUM programm did not uncover an identical previously published disorder. Burn et al. [1986] reported on two Turkish sibs with unlayered polymicrogyria and intra-

Fig. 2. Hypogenitalism with micropenis and hypoplastic scrotum.

Fig. 3. Adducted thumb.

Fig. 4. MRI sagittal T_1-weighted image shows diffuse polymicrogyria and abnormal extension of the sylvian fissure to the convexity.

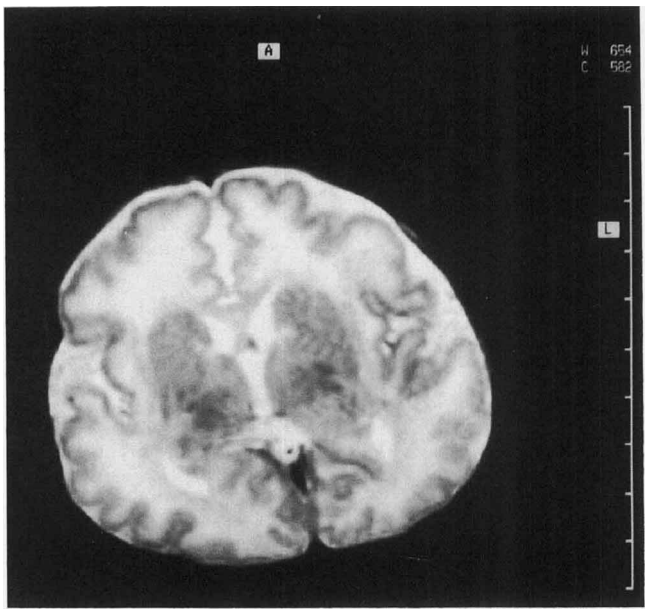

Fig. 5. MRI axial T_2-weighted image shows bilateral incomplete opercularization and diffuse abnormal signal in the white matter.

cerebral calcifications. They also had microcephaly, but no other congenital anomalies.

The occurrence of hereditary turricephaly, microcephaly, and lissencephaly in four affected children from a consanguineous French family was described by Alberca-Serrano and Reznick [1964]. The children had different anomalies including spina bifida, syndactyly and oligophrenia, but none of these children had congenital anomalies as compared to our patient.

Dobyns et al. [1992] described two families with two affected sibs each with lissencephaly and ventilatory-dependent respiratory insufficiency from birth. All died within the first month of life, having remained ventilatory-dependant the entire time. Some had mild contractures, minor facial changes such as narrow palpebral fissures and low set or posteriorly angulated ears. They did not have any other anomalies as described in our patient.

The Winter-Tsukahara syndrome [Winter et al., 1989; Tsukahara et al., 1990; Levin et al., 1993] describes a combination of pachygyria (not better characterized), joint contractures, and facial abnormalities. Some of these anomalies are reminiscent of our patient (Table I),

TABLE I. Comparison of Salient Manifestations in the Winter-Tsukahara Syndrome With the Clinical Traits of Our Patient

Clinical signs	Winter-Tsukahara syndrome	Patient D.P.
Early death	+	+
Turricephaly	–	+
Microbrachycephaly	+	+
Large anterior fontanelle	+	+
Low posterior hair line	–	+
Hypertelorism	+	–
Malformed ears	+	+
Microstomia	–	+
Maxillary retrusion	–	+
Mandibular prognathism	–	+
Progeroid appearance	–	+
Edema of hands and feet	+	–
Redundant skin of neck	+	Decreased subcutaneous fat tissue
Hypoplastic lungs	+	Ventilatory dependence
Cong. heart defect	+	–
Hypoplastic kidney	+	–
Micropenis	+	+
Cryptorchidism	+	+
Camptodactyly	+	+
Distal contractures	+	–
Adducted thumbs	+	+
Diffuse polymicrogyria	–	+
Pachygyria	+	–

including early death, microbrachycephaly, large anterior fontanelle, microgenitalia, and camptodactyly. On the contrary, a number of anomalies present in our patient make it likely that these syndromes are strikingly different. Our patient had a turricephalic head configuration, low posterior hair line, microstomia with maxillary retrusion and mandibular prognathism, and decreased subcutaneous fat tissue as well as a progeroid appearance which was not reported in any of the patients with the Winter-Tsukahara syndrome.

Furthermore, several abnormalities described in the Winter-Tsukahara syndrome such as congenital heart and kidney malformation, hypertelorism, puffiness and edema of hands and feet, distal contractures, and redundant skin of the neck were lacking in our patient.

Our preliminary data show an apparently previously undescribed pattern of diffuse polymicrogyria with abnormal signal in the white matter and multiple congenital anomalies, suggesting a distinct lethal genetic syndrome with a possible autosomal recessive mode of inheritance.

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